

CLAIM AMENDMENTS

1-15. (canceled)

16. (currently amended): A method for preparing a protein containing a modified DDR2 cytosolic tyrosine kinase domain having an increased autophosphorylation and tyrosine kinase activity as compared to said protein containing an unmodified DDR2 cytosolic tyrosine kinase domain, ~~by mutating at least one tyrosine at the DDR2 cytosolic tyrosine kinase domain~~, comprising the steps of:

(a) — amplifying a first DNA fragment which encodes an amino acid sequence ~~sufficiently covering a mutant~~ of the human DDR2 cytosolic tyrosine kinase domain, which is positions 441-885 ~~protein wherein~~ of SEQ ID NO:1, modified such that at least one of tyrosines ~~at the DDR2 cytosolic tyrosine kinase domain~~ positions 736, 740 or 741 has been ~~independently mutated to~~ replaced by phenylalanine, alanine or glycine, ~~by site-directed mutagenesis~~;

— introducing the amplified DNA fragment into a first viral expression vector to construct a recombinant viral expression ~~vector~~ system for said ~~mutant~~ protein comprising the modified DDR2 cytosolic tyrosine kinase domain; and

— generating a first recombinant virus ~~carrying~~ comprising said expression system ~~mutant DDR2 cytosolic tyrosine kinase domain~~;

(b) — amplifying a second DNA fragment which encodes an amino acid sequence of c-Src or c-Src related protein;

— introducing the amplified DNA fragment into a second virus expression vector, to construct a recombinant virus expression system for said Src of Src related protein; and

— generating a second recombinant virus comprising said expression system;

— infecting said first and second recombinant virus into a host cell, ~~to produce the mutant DDR2 cytosolic tyrosine kinase domain~~ co-produce said proteins, and

— inducing tyrosine phosphorylation at the DDR2 cytosolic tyrosine kinase domain by the tyrosine kinase activity of c-Src or c-Src related protein, to produce a protein containing the DDR2 cytosolic tyrosine kinase domain with increased tyrosine phosphorylation;

— isolating and purifying said ~~mutant DDR2 cytosolic tyrosine kinase domain~~ protein containing the DDR2 cytosolic tyrosine kinase domain with increased tyrosine phosphorylation.

17. (currently amended): The method of claim 16, wherein the DDR2 cytosolic tyrosine kinase domain containing protein is tagged with a glutathione-S-transferase tag, a thioredoxin tag or a histidine oligomer tag.

18. (previously presented): The method of claim 16, wherein the virus is a baculovirus and the host cell is an insect cell.

19. (canceled)

20. (currently amended): The method of ~~claim 14~~ claim 16, wherein tyrosine 740 is ~~mutated to~~ replaced by phenylalanine, alanine or glycine.

21-22. (canceled)

23. (new): The method of claim 14, the c-Src related protein is selected from the group consisting of v-Src, Fyn, Yes, Lck, Hck, Lyn, Csk and Blk including their tyrosine kinase-activated versions.

24. (new): A method for preparing a protein containing a modified DDR2 cytosolic tyrosine kinase domain having an increased autophosphorylation and tyrosine kinase activity as compared to said protein containing an unmodified DDR2 cytosolic tyrosine kinase domain, comprising the steps of:

— infecting a host cell with a first virus that comprises an expression system for a protein comprising human DDR2 cytosolic tyrosine kinase domain, which is positions 441-885 of SEQ ID

NO:1, modified such that at least one of tyrosines at positions 736, 740 or 741 has been replaced by phenylalanine, alanine or glycine, and with a second virus that comprises an expression system for a Src or Src related protein to co-produce said proteins;

— inducing tyrosine phosphorylation at the DDR2 cytosolic tyrosine kinase domain by the tyrosine kinase activity of c-Src or c-Src related protein, to produce a protein containing the DDR2 cytosolic tyrosine kinase domain with increased tyrosine phosphorylation;

— isolating and purifying said protein, containing the DDR2 cytosolic tyrosine kinase domain with increased tyrosine phosphorylation.

25. (new): The method of claim 24, wherein the DDR2 cytosolic tyrosine kinase domain containing protein is tagged with a glutathione-S-transferase tag, a thioredoxin tag or a histidine oligomer tag.

26. (new): The method of claim 24, wherein the virus is a baculovirus and the host cell is an insect cell.

27. (new): The method of claim 24, wherein tyrosine 740 is replaced by phenylalanine, alanine or glycine.

28. (new): The method of claim 24, the c-Src related protein is selected from the group consisting of v-Src, Fyn, Yes, Lck, Hck, Lyn, Csk and Blk including their tyrosine kinase-activated versions.

29. (new): A protein containing a modified human DDR2 cytosolic tyrosine kinase domain having an increased autophosphorylation and tyrosine kinase activity as compared to said protein comprising an unmodified cytosolic tyrosine kinase domain, wherein at least one of tyrosine at protein 736, 740 or 741 in the activation loop of the human DDR2 cytosolic tyrosine kinase domain, which is positions 441-885 of SEQ ID NO:1, is replaced by phenylalanine, alanine or glycine.

30. (new): The protein of claim 29, wherein tyrosine 740 is modified.
31. (new): The protein of claim 30, wherein tyrosine 740 is replaced by phenylalanine.